

**WE CLAIM:**

1. An anti-proliferative substance for preventing uncontrolled cellular proliferation, which comprises a radiolabeled DNA carrier, wherein a radioisotope is located internally within the DNA sequence, at 5' end or at 3' end, and wherein said radiolabeled DNA carrier penetrates cell membrane and is retained intracellularly for a time sufficient for the radioisotope to effect an efficient dose therapy.
2. The anti-proliferative substance according to Claim 1, wherein said carrier is an oligonucleotide.
3. The anti-proliferative substance according to Claim 2, wherein said oligonucleotide is linear.
4. The anti-proliferative substance according to Claim 1, wherein said carrier is a plasmid.
5. The anti-proliferative substance according to Claim 4, wherein said plasmid is circular.
6. The anti-proliferative substance according to Claim 5, wherein said plasmid is of viral or bacterial origin.
7. The anti-proliferative substance according to Claim 1, wherein said radioisotope is selected from the group consisting of  $^{32}\text{P}$ ,  $^{33}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ ,  $^{198}\text{Au}$ ,  $^{90}\text{Y}$ ,  $^{89}\text{Sr}$ ,  $^{186}\text{Re}$ ,  $^{45}\text{Ca}$  and  $^{153}\text{Sm}$ .
8. The anti-proliferative substance according to Claim 3, wherein said oligonucleotide is a double-

stranded DNA sequence or a single-stranded DNA sequence.

9. The anti-proliferative substance according to Claim 3, wherein said oligonucleotide is conjugated with an antibody for cell-specific delivery.

10. The anti-proliferative substance according to Claim 8, wherein said DNA oligonucleotide sequence is a single-stranded sense DNA sequence for hybridization to a specific genetic target.

11. The anti-proliferative substance according to Claim 8, wherein said DNA oligonucleotide sequence is a single-stranded antisense DNA sequence for hybridization to a specific genetic target.

12. The anti-proliferative substance according to Claim 1, which comprises DNA sequences of at least about 2 to about 2000 nucleotides.

13. The anti-proliferative substance according to Claim 12, wherein the DNA sequence is selected from the group consisting of

CAC GTT GAG GGG CAT (SEQ ID NO:1)  
ATG CCC CTC AAC GTG (SEQ ID NO:2)  
GCC CGA GAA CAT CAT (SEQ ID NO:3)  
CCT CGC AGT TTC CAT (SEQ ID NO:4)  
AAA AAA AAA AAA AAA TTT (SEQ ID NO:8)  
TTT TTT TTT TTT TTT AAA (SEQ ID NO:9)  
CCC CCC CCC CCC CCC GGG (SEQ ID NO:10)  
CC GCG ACG ATG CCC CTC AAC GTT ACC ATC ACC (SEQ ID NO:11)

wherein the radioisotope is located at any internal position in the sequence.

FIG. 1

1/2 2nd  
part of claim 13

14. The anti-proliferative substance according to Claim 3, wherein the oligonucleotide is conjugated to at least one selected from the group consisting of a stent surface, cholesterol, oleic acid, linoleic acid, TGF $\alpha$ , antibody, TGF $\beta$ , cytokines and growth factors.

15. The anti-proliferative substance according to Claim 13, wherein the radioisotope is selected from the group consisting of  $^{32}\text{P}$ ,  $^{33}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ ,  $^{198}\text{AU}$ ,  $^{90}\text{Y}$ ,  $^{89}\text{SR}$ ,  $^{186}\text{Re}$ ,  $^{45}\text{Ca}$  and  $^{153}\text{Sm}$ .

16. A method for preparing a radiolabeled DNA carrier sequence wherein a radioisotope is located internally within the DNA sequence, which comprises the steps of:

- a) synthesizing a DNA sequence in at least two parts;
- b) labeling the 5' end of one of said two parts with a radioisotope;
- c) hybridizing said two parts of step b) with a sequence capable of hybridizing under stringent conditions; and
- d) ligating together said hybridized two parts.

17. The method of Claim 16, which further include a step e) after step d) to obtain a single-stranded radiolabeled DNA carrier, which comprises

- e) separating the hybridized DNA and recovering the radiolabeled DNA carrier sequence.

18. The method of Claim 12, which further include a step f) after step e) to obtain a double-stranded carrier having both strand radiolabeled, which comprises:

19. The method of Claim 18, wherein said radioisotope is selected from the group consisting of  $^{32}\text{P}$ ,  $^{33}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ ,  $^{198}\text{Au}$ ,  $^{90}\text{Y}$ ,  $^{89}\text{Sr}$ ,  $^{186}\text{Re}$ ,  $^{45}\text{Ca}$  and  $^{153}\text{Sm}$ .

21. The method of Claim 18, wherein said two parts of step a) form a sense sequence and said sequence capable of hybridizing of step c) is a corresponding antisense sequence.

23. Method according to Claim 22, wherein said uncontrolled cell proliferation is a restenosis following angioplasty, and said therapeutic substance is delivered by site-specific intravascular delivery.

25. Method according to Claim 22, wherein said uncontrolled cell proliferation is cancer or a

malignant tumor, and said therapeutic substance is coupled to a peptide moiety.

26. Method according to Claim 25, wherein said peptide moiety is selected from the group consisting of an antibody, TGF $\alpha$ , TGF $\beta$ , cytokines and any growth factors.